IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Jia-He Li and Jie Zhang	Examiner:	Wang, Shengjun
Serial No.:	09/182,645	Group Art Unit:	1617
Filed:	October 30, 1998	Docket No.:	70003.0001US01
Title:	Pharmaceutical Compositions Containing Poly(ADP-Ribose) Glycohydrolase Inhibitors and Methods of Using Same		

APPELLANTS' SUPPLEMENTAL APPEAL BRIEF

BOX AF
Commissioner for Patents
Washington, D.C. 20231

Dear Commissioner:

A Notice of Appeal was filed in this application on March 1, 2002. Appellants' brief was filed on May 10, 2002. In an office action mailed on August 7, 2002, the Examiner reopened prosecution and raised two new grounds of rejection: an enablement rejection under Section 112; and an obviousness rejection, which cites two new references. This supplemental brief is filed in conjunction with Appellants' Request for Reinstatement of the Appeal.

Appellants rely on and incorporate by reference herein its entire Appellant Brief, appendix, and exhibits. The issues previously presented and argued are still relevant and addressed in Sections VI and VIII of the Appeal Brief. The following argument concerns only the two new grounds of rejection, using section headings consistent with the Appeal Brief.

VI. Supplemental Issues Presented on Appeal

The supplemental issues presented for this appeal are (3) whether one of skill in the art would determine that claims 46-49 directed to a method of administrating PARG inhibitors are

enabled; and (4) whether claims 46-49 are rendered obvious by Wang or Ning and Tanuma, in further view of Kim et al. and Wen et al.

VIII. Argument

D. Claims 46-49 to PARG Inhibitors are Enabled

Claims 46-49 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking an enabling disclosure. This new ground of objection was raised for the first time in the Examiner's August 7, 2002 office action. For the reasons presented below, Appellants submit that this late rejection is without merit.

The Examiner in the August 7 Office Action asserted that the claims are enabled for the PARG inhibitors disclosed in the specification, but are not enabled for all PARG inhibitors. The Examiner apparently based this assertion on the contention that "PARG inhibitor" is functional language and that the specification failed to provide guidance with respect to the structural features of a PARG inhibitor. The Examiner further stated that functional language "at the point of novelty" fails to meet the requirements of the first paragraph of 35 U.S.C. § 112, citing University of California v. Eli Lilly & Co, 119 F.3d 1559 (Fed. Cir. 1997) ("Lilly") and General Electric Co. v. Wabash Appliance Corp., 304 U.S. 364 (1937) ("General Electric").

The specification provides an enabling disclosure adequate for one of skill in the art to practice the claimed method using any PARG inhibitor. The specification teaches that several structurally unrelated PARG inhibitors are sufficient to produce the desired effects. See, e.g., Specification, pgs. 25-29 (teaching PARG inhibitors such as glucose derivatives, lignin glycosides, hydrolysable tannins including gallotannins and ellagitannins, adenoside derivatives, acridine derivatives including 6, 9-diamino-2-ethoxyacridine lactate monohydrate, tilorone analogs including tilorone R10.556, daunomycin or daunorubicin hydrochloride, ellipticine,

proflavine, etc.). Accordingly, the specification teaches that any PARG inhibitor, regardless of its structure, can be used in the claimed method. For this reason, one skilled in the art would not consider the specification deficient as to providing guidance as to what structural features are needed to be a PARG inhibitor useful for the claimed method, as they would recognize that any PARG inhibitor will do.

The specification also teaches one of skill in the art exactly what other compounds or agents qualify as a PARG inhibitor. The teaching is hardly surprising: those compounds or agents that function as a PARG inhibitor. Such treatment is described in Example 35, wherein the Appellants set up a PARG enzymatic assay, quantify PARG activities, and determine inhibition constants. (Specification, Example 35, pgs. 101-105; see also pgs. 57-78). Thus, the explicit disclosure and teachings regarding PARG inhibitors is directly contrary to the Examiner's misguided accusation that "the search of PARG inhibitors . . . [is] a pure fishing expedition." Armed with the knowledge of nearly two decades of known PARG inhibitors, the dozens of PARG inhibitors disclosed in the application, and the testing procedures to identify additional PARG inhibitors, one of skill in the art would not be required to perform undue experimentation to use the claimed invention.

The Examiner incorrectly supports his faulty assumptions regarding PARG inhibitors with so-called "functional language at the point of novelty" cases. In doing so, the Examiner confuses the present method claims with product claims. The present invention is not directed to PARG inhibitors, but to a novel and unobvious use of PARG inhibitors. Thus, the Examiner incorrectly asserts functional language is directed to the point of novelty. The point of novelty of the claimed invention is not the structural features of a PARG inhibitor, but rather the use of a

PARG inhibitor, regardless of structure, in treatment of neural and cardiac tissue damage resulting from certain diseases and conditions.

The Examiner's confusion between method claims and product claims is manifest by the Lilly and General Electric cases cited by the Examiner. Product or composition of matter claims were at issue in both Lilly and General Electric. The claims at issue in Lilly were directed to recombinant DNA or recombinant organisms. Lilly, 119 F.3d at 1563. In General Electric the patent was directed to a tungsten filament for incandescent lamps. General Electric, 304 U.S. at 365 ("The patent . . . contains process and product claims; only the later are here involved").

The structure of the product or composition in both of these cited cases was directly the point of novelty, and the courts correctly stated that additional structural features were required. However, structure is not at the point of novelty in the presently claimed method. Rather, as indicated above, structural features are not particularly important in the claimed method. Any PARG inhibitor, regardless of structure, would be recognized as sufficient to practice the presently claimed invention. The Examiner's reliance on Lilly and General Electric is misplaced in relation to the present application.

In summary, the specification provides adequate guidance to one of skill in the art to make and use the invention. One of skill in the art would recognize from the specification that any inhibitor of PARG, regardless of structure, would be expected to be useful in the claimed method. What qualifies as a PARG inhibitor is amply described in the specification. As such a skilled artisan would not recognize the point of novelty as being structural features of PARG inhibitors, but rather as being the use of PARG inhibitors to treat neural and cardiac tissue damage resulting from certain diseases and conditions.

E. The Claims are Patentable Over Wang or Ning, in view of Tanuma AB or AC, and in further view of Kim and Wen

The second new ground of rejection raised in reopening prosecution cites additional secondary or tertiary references (Kim et al., J. Pharm. Soc. Korea, 32, 70-79 (1988) and Wen et al., Acta Neuropathol, 91, 15-22 (1996)) in support of the Examiner's obviousness rejection.[1] Both Kim and Wen take a portion of a ginseng root and appear to test that portion for its effect on global myocardial ischemia and reperfusion (Kim) and for possible neuroprotective activity (Wen). These articles concerning ginseng—like Wang and Ning—simply do not disclose or teach a PARG inhibitor.

The addition of Kim and Wen to the Examiner's obviousness rejection does not bolster the Examiner's position. Rather, the addition of these references, in particular Wen, weakens the Examiner's position.

As noted in Appellants' Brief, in discussing the obviousness rejection based on Wang, Ning, and Tanuma, there are at least dozens if not hundreds of distinct compounds/agents in any one type of ginseng, and there are many different types of ginseng. Moreover, there is no consensus among those of ordinary skill in the art as to which particular component of ginseng may have a health benefit—if indeed ginseng has any particular health benefit whatsoever.

The Examiner is apparently citing Wang and Ning for their alleged teaching that ginseng, in the form of tea, can be used to treat ischemia and diabetes. The Examiner cites Tanuma for the proposition that ginseng can contain lignin glycoside, a PARG inhibitor. From this, the Examiner asserts that the ginseng tea of Wang and Ning unequivocally contained lignin glycoside and that the lignin glycoside in the tea unequivocally results in treatment of diabetes

[1] Appellants are unable to determine from the August 7, 2002 office action whether the Examiner is citing Kim et al. and Wen et al. as secondary or tertiary references.

and ischemia. The incorrect nature of this assertion has been addressed in Appellants' Brief. Nothing in Wang or Ning indicates that, of the many possible compounds or combinations of compounds present in their ginseng teas, lignin glycoside or any other PARG inhibitor is responsible for the alleged effect of the ginseng tea.

The Examiner does not explain what relevance the ginseng tested in Kim and Wen has to claims 46-49. (See August 7, 2002 Action, pgs. 6-7). However, neither reference overcomes the deficiencies of the combination of Wang, Ning, and Tanuma. There is absolutely no evidence in Wen and Kim that the portions of ginseng tested contained PARG inhibitors or that PARG inhibitors were responsible for the effects observed. In fact, Kim suffers from the same deficiency as Wang and Ning, as Kim disclosed whole ginseng rather than identifying which isolated compound(s) are responsible for the reported protective effect against ischemic-reperfused heart condition.

While Wen does teach which compound may be responsible for the disclosed neuroprotective effect, Wen teaches away from the presently claimed invention. Wen tests three isolated purified compounds from the ginseng root (Rb_1, Rg_1, and Ro), none of which have the structure of a known PARG inhibitor or of lignin glycoside. Of the three tested, isolated and purified compounds, Wen discloses that Rb_1, which is a ginseng saponin of the protopanaxadiol group, had neuroprotective effects in gerbils with 5-minute forebrain ischemia. As Rb_1, a protopanaxadiol ginseng saponin, does not have the structure of a known PARG inhibitor or of lignin glycoside, Wen would lead one of skill in the art away from the invention claimed in claims 46-49. That is, Wen would lead the skilled artisan to study additional protopanaxadiol ginseng saponins, rather than PARG inhibitors, to identify compounds having neuroprotective effects.

There is simply no connection that one of skilled in the art can make between ginseng and claims 46-49. The Examiner's unwarranted reading of this claim limitation (i.e., a PARG inhibitor) into Wang, Ning, Tanuma, Kim, and Wen should be disregarded.

Applicants respectfully request that the Board reverse all of the obviousness rejections.

IX. Conclusion

For the foregoing reasons, the rejections of Claims 46-49 should be reversed.

Respectfully submitted,

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